

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
 NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
 NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 4 Apr 09 ZDB will be removed from STN
 NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
 NEWS 9 Jun 03 New e-mail delivery for search results now available
 NEWS 10 Jun 10 MEDLINE Reload
 NEWS 11 Jun 10 PCTFULL has been reloaded
 NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
 NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
 saved answer sets no longer valid
 NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
 NEWS 15 Jul 30 NETFIRST to be removed from STN
 NEWS 16 Aug 08 CANCERLIT reload
 NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18 Aug 08 NTIS has been reloaded and enhanced
 NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
 now available on STN
 NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
 NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
 NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
 NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
 NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
 NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
 CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
 AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS STN Operating Hours Plus Help Desk Availability
 NEWS INTER General Internet Information
 NEWS LOGIN Welcome Banner and News Items
 NEWS PHONE Direct Dial and Telecommunication Network Access to STN
 NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:21:20 ON 04 OCT 2002

=> file reg

| | | |
|----------------------|------------------|---------------|
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 14:21:36 ON 04 OCT 2002

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 OCT 2002 HIGHEST RN 459123-02-5
DICTIONARY FILE UPDATES: 3 OCT 2002 HIGHEST RN 459123-02-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See [HELP CROSSOVER](#) for details.

Experimental and calculated property data are now available. See [HELP PROPERTIES](#) for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

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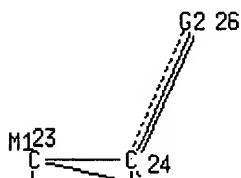
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L1 HAS NO ANSWERS

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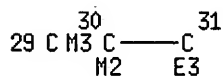
20 C M2

Page 1-A

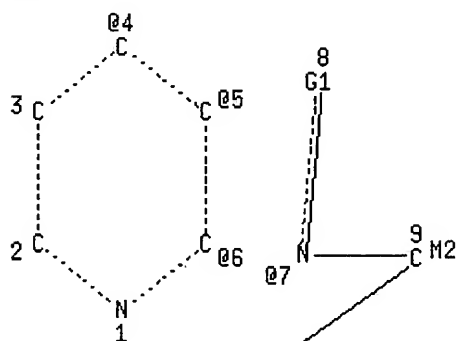


Page 1-B

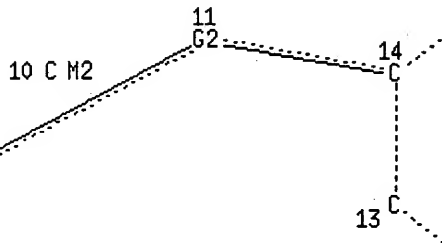
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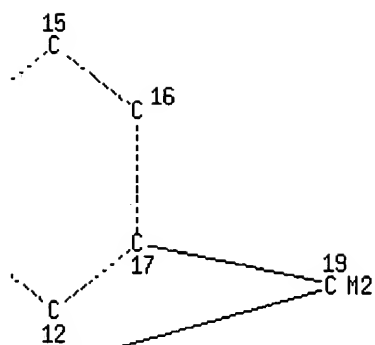


Page 1-D

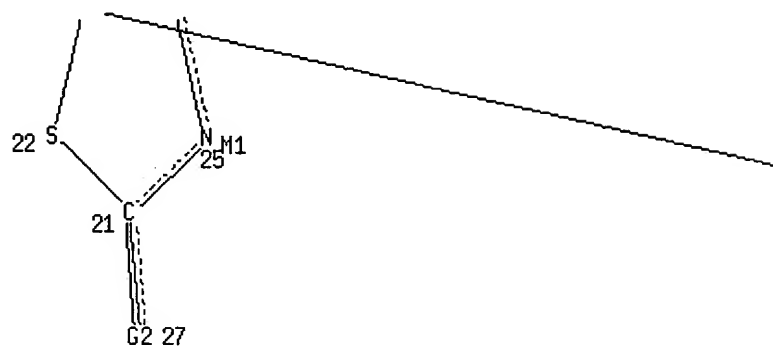


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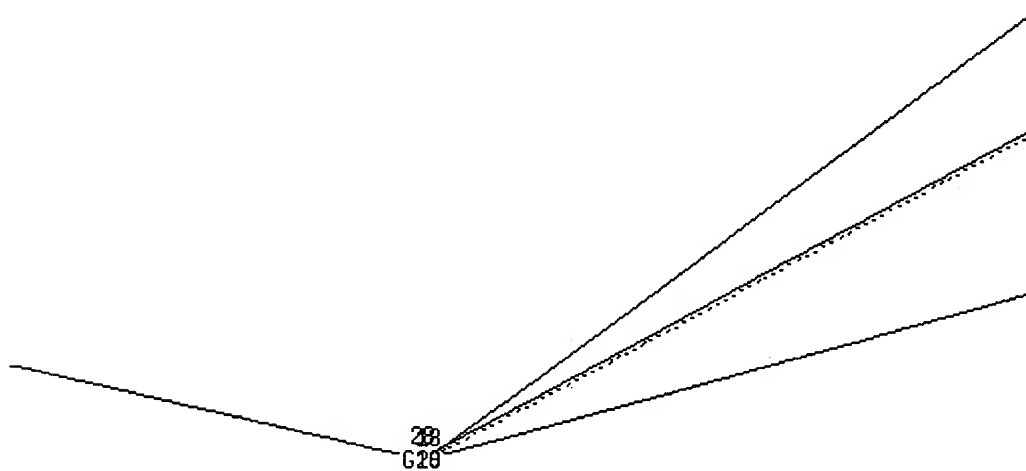


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Page 2-C



Page 2-D

Page 2-E

Page 2-F

VAR G1=29/30

VAR G2=32/33

REP G19=(0-1) 20-19 20-23

REP G20=(0-1) 10-9 10-11

VPA 7-4/5/6 S

NODE ATTRIBUTES:

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DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 7 9 10 19 20 29 30 31 32 33

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE

=> s l1

SAMPLE SEARCH INITIATED 14:22:37 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 10 TO ITERATE

100.0% PROCESSED 10 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.04

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11 TO 389
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s l1 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 139.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 14:22:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 310 TO ITERATE

100.0% PROCESSED 310 ITERATIONS 48 ANSWERS
SEARCH TIME: 00.00.07

L3 48 SEA SSS FUL L1

=> file hcaplus

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 140.66 | 140.87 |

FILE 'HCAPLUS' ENTERED AT 14:23:03 ON 04 OCT 2002
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FILE COVERS 1907 - 4 Oct 2002 VOL 137 ISS 15
FILE LAST UPDATED: 3 Oct 2002 (20021003/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l3

L4 490 L3

=> s 14 and hydra?

352752 HYDRA?

L5 14 L4 AND HYDRA?

=> d 15, ibib abs fhitstr, 1-14

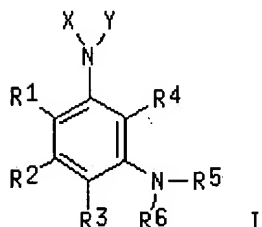
L5 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Citing
Text References

ACCESSION NUMBER: 2002:637641 HCAPLUS
DOCUMENT NUMBER: 137:169309
TITLE: Preparation of substituted aminobenzene derivatives as glucocorticoid receptor modulators
INVENTOR(S): Link, James T.; Sorensen, Bryan K.; Patel, Jyoti R.; Arendsen, David L.; Li, Gaoquan
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2002064550 | A1 | 20020822 | WO 2002-US4501 | 20020212 |
| W: CA, JP, MX | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |

PRIORITY APPLN. INFO.: US 2001-783636 A 20010214
OTHER SOURCE(S): MARPAT 137:169309
GI



AB Gen, hydroxyalkyl, substituted amine; R4 is substituted aminobenzenes I were prepd. and are novel glucocorticoid receptor modulators and are useful for treating type II diabetes in a mammal, wherein R1-R3 are each independently hydrogen, alkoxycarbonyl, alkoxy, alkoxyalkyl, alkyl, alkylcarbonyl, carboxy, halogen, hydroxyalkyl, substituted amine; R4 is hydrogen, alkenyl, alkoxy, alkoxyalkenyl, alkoxyalkoxy, alkoxyalkyl, alkoxyalkynyl, alkoxycarbonyl, alkoxycarbonylalkoxy, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkoxycarbonylalkynyl, alkyl, alkylcarbonyl, alkylcarbonylalkenyl, alkylcarbonylalkoxy, alkylcarbonylalkyl, alkylcarbonylalkynyl, alkynyl, carboxy, carboxyalkenyl, carboxyalkyl, carboxyalkynyl, haloalkoxy, haloalkyl, haloalkenyl, haloalkynyl, halogen, hydroxyalkyl, substituted amine; R5 is hydrogen, alkyl; R6 is hydrogen, alkoxycarbonyl, alkoxysulfonyl, alkyl, alkylcarbonyl, alkylsulfonyl, arylalkoxycarbonyl, arylalkylcarbonyl, arylalkylsulfonyl, arylcarbonyl, arylsulfonyl, cycloalkylcarbonyl, cycloalkylalkylcarbonyl, cycloalkylsulfonyl, cycloalkylalkylsulfonyl, heterocyclecarbonyl, heterocyclealkylcarbonyl, heterocyclesulfonyl, heterocyclealkylsulfonyl, amide, aminosulfonyl; X and Y are independently heteroatom-contg. hydrocarbon. Thus, N-[3-(dibenzylamino)-2-methylphenyl]ethanesulfonamide was prepd. as glucocorticoid receptor

modulator. A method of treating symptoms related to type II diabetes wherein said symptoms are selected from the group consisting of hyperglycemia, hyperinsulinemia, inadequate, glucose clearance, obesity, hypertension and high glucocorticoid levels in a mammal comprising administering a therapeutically effective amt. of a compd. of title compds. A method of treating diseases assocd. with an excess or deficiency of glucocorticoids, said diseases selected from the group consisting of diabetes, obesity, Syndrome X, Cushing's Syndrome, Addison's disease, inflammatory diseases such as asthma, rhinitis and arthritis, allergy, autoimmune disease, immunodeficiency, anorexia, cachexia, bone loss or bone frailty, and wound healing comprising administering a therapeutically effective amt. of a compd. of title compds.

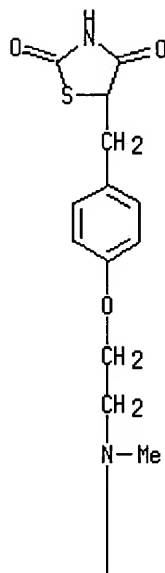
IT **122320-73-4**, Rosiglitazone

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of substituted aminobenzene derivs. as glucocorticoid receptor modulators)

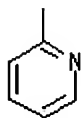
RN **122320-73-4** HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

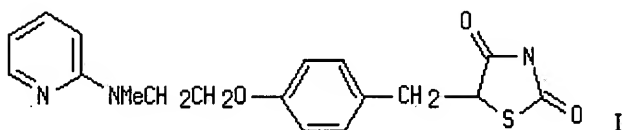
L5 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:904164 HCAPLUS
DOCUMENT NUMBER: 136:20065
TITLE: 5-[4-[2-(Methyl-2-pyridylamino)ethoxy]benzyl]thiazolidine-2,4-dione hydriodide as pharmaceutical
INVENTOR(S): Craig, Andrew Simon; Ho, Tim Chien Ting; Millan, Michael John

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2001094343 | A1 | 20011213 | WO 2001-GB2545 | 20010608 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | GB 2000-14005 | A 20000608 |
| GI | | | | |



AB The title compd. (I·HI) is prepd. by refluxing I with HI in various solvents (2-propanol, THF, toluene, etc.). The hydriodide **hydrate** is also prepd. and x-ray powder diffraction patterns are provided. I·HI is indicated to be useful in the treatment and/or prophylaxis of diabetes mellitus and certain of its complications.

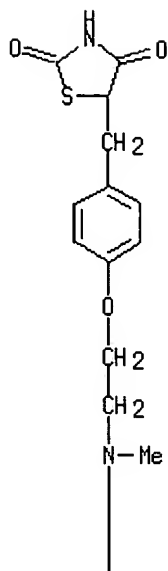
IT 122320-73-4

RL: RCT (Reactant); RACT (Reactant or reagent)
 (conversion to hydriodide)

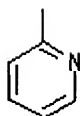
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:816444 HCAPLUS
 DOCUMENT NUMBER: 135:352829
 TITLE: Combination therapeutic compositions containing benzene compounds
 INVENTOR(S): Jaen, Juan C.; Chen, Jin-Long
 PATENT ASSIGNEE(S): Tularik Inc., USA
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001082916 | A2 | 20011108 | WO 2001-US14393 | 20010502 |
| WO 2001082916 | A3 | 20020704 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002037928 | A1 | 20020328 | US 2001-847887 | 20010502 |

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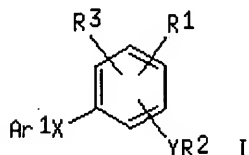
US 2000-201613P

P 20000503

OTHER SOURCE(S):

MARPAT 135:352829

GI



AB The present invention provides pharmaceutical compns. and methods for the treatment of diabetes mellitus using combination therapy. The compns. relate to a benzene compd. and an antidiabetic agent such as sulfonylureas, biguanides, glitazones, α -glucosidase inhibitors, potassium channel antagonists, aldose reductase inhibitors, glucagon antagonists, activators of RXR, insulin therapy or other anti-obesity agent. The methods include the administration of the combination of benzene compd. with antidiabetic agent where the two components are delivered in a simultaneous manner, where the benzene compd. is administered first, followed by the antidiabetic agent, as well as wherein the antidiabetic agent is delivered first followed by the benzene compd. For example, the benzene compd. (I) was synthesized using a 5-amino-2-(3-chloro-5-pyridyloxy)benzonitrile (0.457 g) in methylene chloride to which was added 2,4-dichlorobenzenesulfonyl chloride (0.456 g), followed by pyridine (150 μ L). The reaction progress was monitored by TLC, and upon completion the solvent was removed under vacuum. The resulting residue was partitioned between methylene chloride and water. The org. layer was drawn off and concd. The residue was triturated with ether to provide 0.447 g of I as a white solid, m.p. 154-156°.

IT 122320-73-4, Rosiglitazone

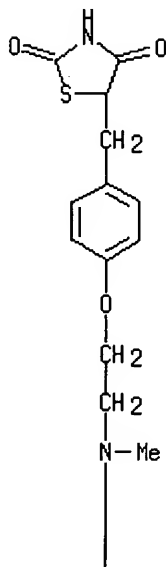
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzene compds. in combination therapy for diabetes and diabetes-related disorders)

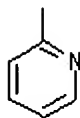
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L5 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2002 ACS

| Full Text | Citing References |
|--------------|----------------------|
|--------------|----------------------|

ACCESSION NUMBER: 2001:780683 HCAPLUS
 DOCUMENT NUMBER: 135:335156
 TITLE: Modified-release formulations containing a hypnotic agent
 INVENTOR(S): Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria
 PATENT ASSIGNEE(S): Synthon B.V., Neth.
 SOURCE: PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2001078725 | A2 | 20011025 | WO 2001-NL299 | 20010412 |
| WO 2001078725 | A3 | 20011220 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-196939P P 20000413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem hydrochloride hydrate 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

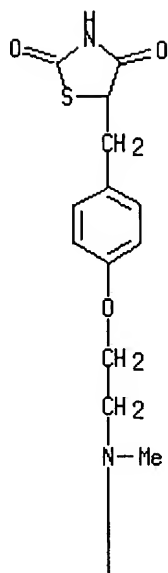
IT 122320-73-4, Rosiglitazone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (modified-release formulations contg. hypnotic agent)

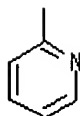
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L5 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:693320 HCAPLUS
 DOCUMENT NUMBER: 135:247196
 TITLE: Preparation of non-hygroscopic hydrochloride salts of 5-[4-[2-(n-methyl-n-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione
 INVENTOR(S): Craig, Andrew Simon
 PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001068646 | A1 | 20010920 | WO 2001-GB1131 | 20010314 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 2000-6133 A 20000314
 AB A substantially non-hydrated and non-hygroscopic or slightly hygroscopic hydrochloride salts of 5-[4-[2-(N-methyl-N-(2-

pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I); a pharmaceutical compn. contg. such a compd., a process of prepg. such a compd. and the use of such a compd. in medicine is disclosed. I was prepd. by the reaction of HCl with the base, m.p. = 167-170. I was non-hygroscopic.

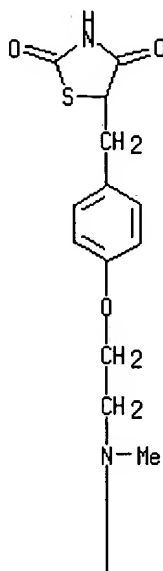
IT **302543-62-0P**

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-hygroscopic hydrochloride salts of
pyridylaminoethoxybenzyl thiazolidinedione)

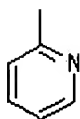
RN 302543-62-0 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:584706 HCAPLUS
DOCUMENT NUMBER: 135:352600
TITLE: Peroxisome proliferator-activated receptor subtype-specific regulation of hepatic and peripheral gene expression in the Zucker diabetic fatty rat
AUTHOR(S): Dana, Sharon L.; Hoener, Patricia A.; Bilakovics, James M.; Crombie, Diane L.; Ogilvie, Kathleen M.; Kauffman, Raymond F.; Mukherjee, Ranjan; Paterniti, James R., Jr.
CORPORATE SOURCE: Department of Pharmacology, Ligand Pharmaceuticals,

SOURCE: Inc., San Diego, CA, 92121, USA
Metabolism, Clinical and Experimental (2001), 50(8), 963-971
CODEN: METAAJ; ISSN: 0026-0495

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

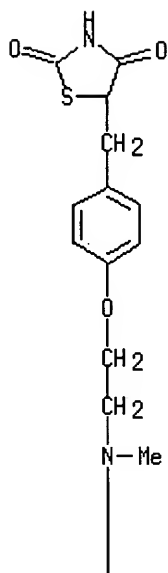
AB Fibrates and thiazolidinediones are used clin. to treat hypertriglyceridemia and hyperglycemia, resp. Fibrates bind to the peroxisome proliferator-activated receptor (PPAR)- α , and thiazolidinediones are ligands of PPAR- γ . These intracellular receptors form heterodimers with retinoid X receptor to modulate gene transcription. To elucidate the target genes regulated by these compds., we treated Zucker diabetic fatty rats (ZDF) for 15 days with a PPAR- α -specific compd., fenofibrate, a PPAR- γ -specific ligand, rosiglitazone, and a PPAR- α / γ coagonist, GW2331, and measured the levels of several mRNAs in liver by real-time polymerase chain reaction. All 3 compds. decreased serum glucose and triglyceride levels. Fenofibrate and GW2331 induced expression of acyl-CoA (CoA) oxidase and enoyl-CoA hydratase and reduced apolipoprotein C-III and phosphoenolpyruvate carboxykinase mRNAs. Rosiglitazone modestly increased apolipoprotein C-III mRNA and had no effect on expression of the other 2 genes in the liver but increased the expression of glucose transporter 4 and phosphoenolpyruvate carboxykinase in adipose tissue. We identified a novel target in liver, mitogen-activated phosphokinase phosphatase 1, whose down-regulation by PPAR- α agonists may improve insulin sensitivity in that tissue by prolonging insulin responses. The results of these studies suggest that activation of PPAR- α as well as PPAR- γ in therapy for type 2 diabetes will enhance glucose and triglyceride control by combining actions in hepatic and peripheral tissues.

IT 122320-73-4, Rosiglitazone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peroxisome proliferator-activated receptor subtype-specific regulation of hepatic and peripheral gene expression in Zucker diabetic fatty rat)

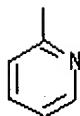
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2001032928 | A2 | 20010510 | WO 2000-US30474 | 20001103 |
| WO 2001032928 | A3 | 20020725 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

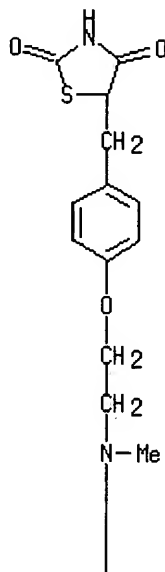
IT 122320-73-4, Rosiglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

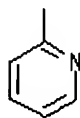
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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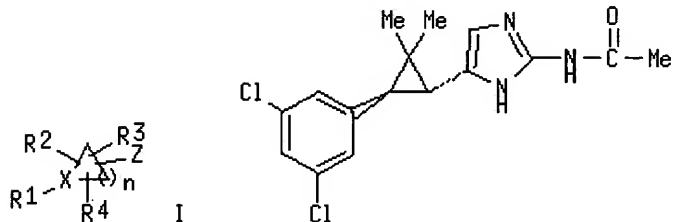
L5 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:283949 HCAPLUS
DOCUMENT NUMBER: 134:311218
TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2001027107 | A2 | 20010419 | WO 2000-US27461 | 20001002 |
| WO 2001027107 | A3 | 20020124 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1224183 | A2 | 20020724 | EP 2000-968723 | 20001002 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| NO 2002001717 | A | 20020610 | NO 2002-1717 | 20020411 |
| PRIORITY APPLN. INFO.: | | | US 1999-158755P | P 19991012 |
| | | | WO 2000-US27461 | W 20001002 |

OTHER SOURCE(S): MARPAT 134:311218
GI



AB Compds. of formula I [wherein; n is 1-5; X is N or CR₅, where R₅ is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R₁ is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R₂, R₃ and R₄ are any of the groups set out for R₁ and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R₁ is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding α-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, β-adrenergic agonists, hypolipidemic

agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **122320-73-4**, Rosiglitazone

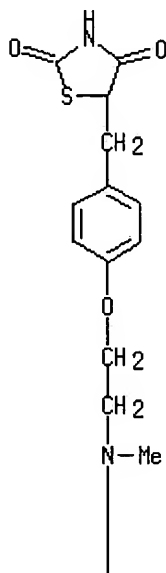
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

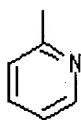
RN **122320-73-4** HCAPLUS

CN **2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)**

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L5 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2002 ACS

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| Full Text | Citing References |
|-----------|-------------------|

ACCESSION NUMBER: 2000:861703 HCAPLUS
 DOCUMENT NUMBER: 134:532
 TITLE: Method and compositions relating to insulin resistance disorders
 INVENTOR(S): Cawthorne, Michael; Sanchez, Jean-Charles
 PATENT ASSIGNEE(S): Proteome Sciences PLC, UK
 SOURCE: PCT Int. Appl., 188 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

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|---|----|----------|----------------|----------|
| WO 2000073330 | A2 | 20001207 | WO 2000-GB2110 | 20000601 |
| WO 2000073330 | A3 | 20010222 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| GB 2350676 | A1 | 20001206 | GB 1999-12741 | 19990601 |
| EP 1185862 | A2 | 20020313 | EP 2000-935377 | 20000601 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.:

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| GB 1999-12741 | A | 19990601 |
| GB 2000-2973 | A | 20000209 |
| WO 2000-GB2110 | W | 20000601 |

AB Methods and compns. relating to insulin resistance are disclosed. Specifically, proteins that are differentially expressed in these conditions are identified. In one aspect, the invention provides a method of screening an agent to det. its usefulness in treating insulin resistance, based on establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having differential levels of insulin sensitivity.

IT 122320-73-4, Brl 49653

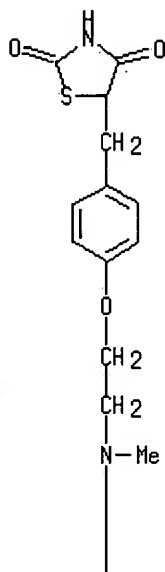
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method and compns. relating to insulin resistance disorders)

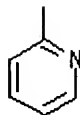
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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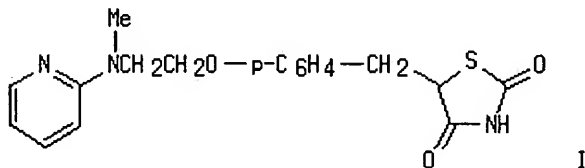
L5 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2002 ACS

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| Full Text | Citing References |
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| ACCESSION NUMBER: | 2000:756704 | HCAPLUS |
| DOCUMENT NUMBER: | 133:325652 | |
| TITLE: | 5-[4-[2-(N-Methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione hydrochloride monohydrate pharmaceutical | |
| INVENTOR(S): | Blackler, Paul David James; Craig, Andrew Simon; Giles, Robert Gordon; Sasse, Michael John | |
| PATENT ASSIGNEE(S): | Smithkline Beecham P.L.C., UK | |
| SOURCE: | PCT Int. Appl., 15 pp. CODEN: PIXXD2 | |
| DOCUMENT TYPE: | Patent | |
| LANGUAGE: | English | |
| FAMILY ACC. NUM. COUNT: | 1 | |
| PATENT INFORMATION: | | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2000063206 | A2 | 20001026 | WO 2000-GB1527 | 20000419 |
| WO 2000063206 | A3 | 20010222 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1173437 | A2 | 20020123 | EP 2000-920895 | 20000419 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 2000009898 | A | 20020416 | BR 2000-9898 | 20000419 |
| NO 2001005105 | A | 20011219 | NO 2001-5105 | 20011019 |
| PRIORITY APPLN. INFO.: | | | GB 1999-9075 | A 19990420 |
| | | | WO 2000-GB1527 | W 20000419 |

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AB 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione hydrochloride monohydrate (I.HCl.H2O) is characterized in that it: (i) provides an IR spectrum contg. peaks at 3358, 2764, 1245, 833 and 760 cm^{-1} ; and/or (ii) provides an XRPD pattern contg. peaks at 15.0, 17.7, 23.0, 30.0 and 31.4 $^{\circ}$ 2 θ . >2303082-83-9P

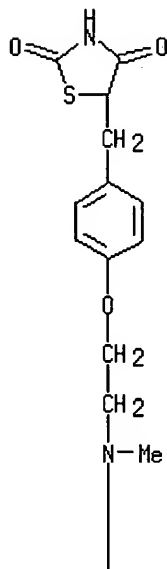
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(5-[4-[2-(N-Methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione hydrochloride monohydrate pharmaceutical)

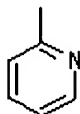
RN 303082-83-9 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monohydrochloride, monohydrate (9CI) (CA INDEX NAME)

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HCl

H₂O

L5 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2002 ACS

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| Full Text | Citing References |
|--------------|----------------------|

ACCESSION NUMBER: 2000:190914 HCAPLUS

DOCUMENT NUMBER: 132:241947

TITLE: Compositions for treatment of glucose metabolism disorders

INVENTOR(S): Fine, Stuart; Kinsella, Kevin

PATENT ASSIGNEE(S): Akesis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
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|----------------------|----|----------|------------------------|----------|
| <u>WO 2000015211</u> | A2 | 20000323 | <u>WO 1999-US21377</u> | 19990917 |
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| <u>WO 2000015211</u> | A3 | 20010329 | | |
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|-------------------|----|----------|-----------------------|----------|
| <u>US 6376549</u> | B1 | 20020423 | <u>US 1998-156102</u> | 19980917 |
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| <u>AU 9960446</u> | A1 | 20000403 | <u>AU 1999-60446</u> | 19990917 |
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| <u>EP 1113804</u> | A2 | 20010711 | <u>EP 1999-969024</u> | 19990917 |
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-156102 A 19980917

US 1999-126489P P 19990326

WO 1999-US21377 W 19990917

AB Compns. and methods of using the same for the treatment of diabetes and other disorders of glucose metab. are provided. Compns. may include an anti-diabetic agent and 1 or more of a bioavailable source of chromium and vanadium. A supplement (detailed below) was administered daily to a female with Type 2 diabetes who was experiencing poor blood sugar control while taking metformin 500 mg b.i.d. In conjunction with continued metformin administration, the patient was given an oral daily nutritional supplement comprising the following ingredients: chromium 333 µg (in the form of chromium picolinate/polynicotinate); magnesium 46 mg (in the form of 384 mg magnesium chloride); vanadyl-sulfate **hydrate** 100 mg; vitamin E 400 IU, and folate 400 µg. In addn. to the lowered HbA1c and fasting blood sugar levels, the patient experienced a significant lowering of total cholesterol and a concomitant lowering of triglyceride, HDL and LDL levels.

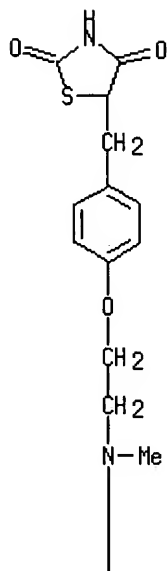
IT 122320-73-4, Rosiglitazone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treatment of glucose metab. disorders)

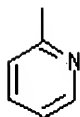
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L5 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2002 ACS

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| Full Text | Citing References |
|--------------|----------------------|

ACCESSION NUMBER: 1999:404959 HCAPLUS

DOCUMENT NUMBER: 131:58818

TITLE: Preparation of a thiazolidinedione derivative as
hydrate for prophylaxis or treatment of diabetes

INVENTOR(S): Blackler, Paul David James; Lee, David C.; Sasse,
Michael John

PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 9931095 | A1 | 19990624 | WO 1998-EP8155 | 19981214 |
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DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2314107 AA 19990624 CA 1998-2314107 19981214

AU 9919679 A1 19990705 AU 1999-19679 19981214

EP 1040110 A1 20001004 EP 1998-964510 19981214

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

BR 9813600 A 20001010 BR 1998-13600 19981214

JP 2002508373 T2 20020319 JP 2000-539019 19981214

ZA 9811506 A 20001106 ZA 1998-11506 19981215

NO 2000003069 A 20000615 NO 2000-3069 20000615

US 2002137940 A1 20020926 US 2002-82879 20020226

PRIORITY APPLN. INFO.: GB 1997-26566 A 19971216

WO 1998-EP8155 W 19981214

US 2000-581826 B1 20000616

AB Prepn. of a **hydrate** of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione maleate (I) for prophylaxis and/or treatment of diabetes mellitus and conditions assocd. with it is described. The compd. comprises water in the range of 0.4-2.5% wt./wt. and provides a specific IR spectrum, an X-ray powder diffraction pattern, a Raman spectrum, and/or a solid-state NMR spectrum. I with the water content of 0.54% wt./wt. was prepd. from 6 g of the I free base and 2.1 g maleic acid salt by heating in MeOH to 55° to obtain a soln.; the soln. was filtered, reheated at 55°, and then cooled to 0-5° and stirred. The product was filtered and dried at 52° in vacuo to give I in 84% yield (6.7 g).

IT 227606-02-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of thiazolidinedione deriv. as **hydrate** for prophylaxis or treatment of diabetes)

RN 227606-02-2 HCAPLUS

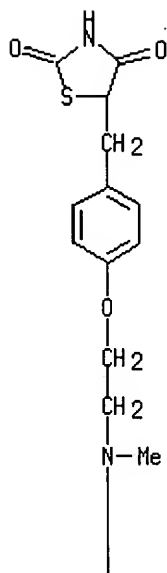
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1), hydrate (9CI) (CA INDEX NAME)

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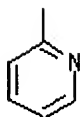
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



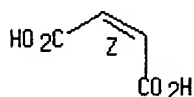
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:404958 HCAPLUS

DOCUMENT NUMBER: 131:63474

TITLE: **Hydrate** of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl]thiazolidine-2,4-dione maleic acid salt

INVENTOR(S): Blackler, Paul David James; Lee, David C.; Sasse, Michael John

PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK

SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| <u>WO 9931094</u> | A1 | 19990624 | <u>WO 1998-EP8154</u> | 19981214 |
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| <u>CA 2314965</u> | AA | 19990624 | <u>CA 1998-2314965</u> | 19981214 |
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| <u>AU 9922723</u> | A1 | 19990705 | <u>AU 1999-22723</u> | 19981214 |
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| <u>BR 9813604</u> | A | 20001010 | <u>BR 1998-13604</u> | 19981214 |
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| <u>EP 1045847</u> | A1 | 20001025 | <u>EP 1998-966321</u> | 19981214 |
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

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| <u>JP 2002508372</u> | T2 | 20020319 | <u>JP 2000-539018</u> | 19981214 |
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| <u>ZA 9811505</u> | A | 20001106 | <u>ZA 1998-11505</u> | 19981215 |
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| <u>TW 467913</u> | B | 20011211 | <u>TW 1998-87121122</u> | 19981216 |
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| <u>NO 2000003068</u> | A | 20000615 | <u>NO 2000-3068</u> | 20000615 |
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| <u>US 2002099081</u> | A1 | 20020725 | <u>US 2002-72096</u> | 20020207 |
|----------------------|----|----------|----------------------|----------|

PRIORITY APPLN. INFO.: GB 1997-26568 A 19971216

WO 1998-EP8154 W 19981214

US 2000-581719 A1 20000616

AB A **hydrate** of the title compd. is prepd. which is useful in treatment and/or prophylaxis of diabetes mellitus and its complications and assocd. conditions such as insulin resistance, impaired glucose tolerance, hyperinsulinemia, obesity, and gestational diabetes, and is particularly suitable for bulk prepn. and handling. The **hydrate** is characterized by a water content of 0.2-1.1 wt.% and by its IR spectrum and x-ray powder diffraction pattern. The **hydrate** is prepd. by crystn. from an aq. alkanol, preferably contg. 2.0-2.5 vol.% water.

IT 227606-02-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**hydrate** of antidiabetic thiazolidinedione deriv.)

RN 227606-02-2 HCAPLUS

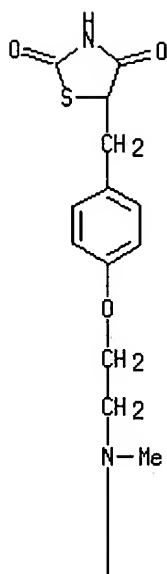
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1), hydrate (9CI) (CA INDEX NAME)

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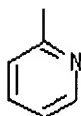
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



PAGE 2-A

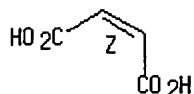


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:404957 HCAPLUS

DOCUMENT NUMBER: 131:49500
 TITLE: Substituted thiazolidinedione derivative and its
 preparation for pharmaceutical use
 INVENTOR(S): Lynch, Ian Robert; Choudary, Bernadette Marie; Sasse,
 Michael John
 PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| <u>WO 9931093</u> | A1 | 19990624 | <u>WO 1998-EP8153</u> | 19981214 |
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 KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
 MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
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 TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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| <u>CA 2314967</u> | AA | 19990624 | <u>CA 1998-2314967</u> | 19981214 |
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| <u>AU 9922722</u> | A1 | 19990705 | <u>AU 1999-22722</u> | 19981214 |
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| <u>BR 9813598</u> | A | 20001010 | <u>BR 1998-13598</u> | 19981214 |
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| <u>EP 1042321</u> | A1 | 20001011 | <u>EP 1998-966320</u> | 19981214 |
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

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| <u>JP 2002508371</u> | T2 | 20020319 | <u>JP 2000-539017</u> | 19981214 |
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| <u>ZA 9811504</u> | A | 20000615 | <u>ZA 1998-11504</u> | 19981215 |
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| <u>NO 2000003070</u> | A | 20000615 | <u>NO 2000-3070</u> | 20000615 |
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| <u>US 2002133016</u> | A1 | 20020919 | <u>US 2002-71339</u> | 20020208 |
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PRIORITY APPLN. INFO.: GB 1997-26563 A 19971216

WO 1998-EP8153 W 19981214

US 2000-581816 A1 20000616

AB A **hydrate** of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl]thiazoli
 dine-2,4-dione maleic acid salt contg. 0.3-0.6 molar equivs. water is
 useful for treatment and/or prophylaxis of diabetes mellitus and assocd.
 conditions and complications. The compd. is characterized by its IR,
 Raman, and NMR spectra and its x-ray powder diffraction pattern. It is
 prepd. by crystg. the anhyd. compd. from aq. EtOH, other aq. solvent
 mixts., or H₂O contg. 2-5 vol.% AcOH or other org. acid, and is esp.
 suitable for bulk prepn. and handling.

IT **227606-02-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(substituted thiazolidinedione deriv. and its prepn. for pharmaceutical use)

RN 227606-02-2 HCAPLUS

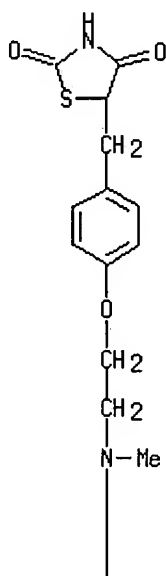
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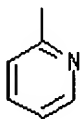
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



PAGE 2-A

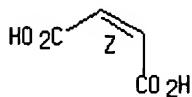


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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| CA SUBSCRIBER PRICE | | -8.67 | -8.67 |

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FILE COVERS 1907 - 4 Oct 2002 VOL 137 ISS 15
FILE LAST UPDATED: 3 Oct 2002 (20021003/ED)

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L3 48 S L1 FULL

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L4 490 S L3
L5 14 S L4 AND HYDRA?

FILE 'HCAPLUS' ENTERED AT 14:25:08 ON 04 OCT 2002

=> s **15 and hydrochloride**
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7153 HYDROCHLORIDES
107959 HYDROCHLORIDE
(HYDROCHLORIDE OR HYDROCHLORIDES)
L6 6 L5 AND HYDROCHLORIDE

=> d l6, **ibib abs fhitr, 1-6**

L6 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Citing
Text References

ACCESSION NUMBER: 2002:637641 HCAPLUS
DOCUMENT NUMBER: 137:169309
TITLE: Preparation of substituted aminobenzene derivatives as
glucocorticoid receptor modulators
INVENTOR(S): Link, James T.; Sorensen, Bryan K.; Patel, Jyoti R.;
Arendsen, David L.; Li, Gaoquan
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| <u>WO 2002064550</u> | A1 | 20020822 | <u>WO 2002-US4501</u> | 20020212 |
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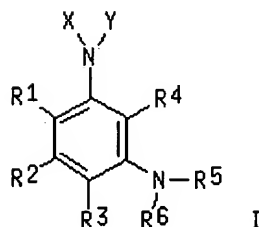
W: CA, JP, MX

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRIORITY APPLN. INFO.: US 2001-783636 A 20010214

OTHER SOURCE(S): MARPAT 137:169309

GI



AB Gen, hydroxyalkyl, substituted amine; R4 is substituted aminobenzenes I were prepd. and are novel glucocorticoid receptor modulators and are useful for treating type II diabetes in a mammal, wherein R1-R3 are each independently hydrogen, alkoxycarbonyl, alkoxy, alkoxyalkyl, alkyl, alkylcarbonyl, carboxy, halogen, hydroxyalkyl, substituted amine; R4 is hydrogen, alkenyl, alkoxy, alkoxyalkenyl, alkoxyalkoxy, alkoxyalkyl, alkoxyalkynyl, alkoxycarbonyl, alkoxycarbonylalkoxy, alkoxycarbonylalkenyl, alkoxycarbonylalkyl, alkoxycarbonylalkynyl, alkyl, alkylcarbonyl, alkylcarbonylalkenyl, alkylcarbonylalkoxy, alkylcarbonylalkyl, alkylcarbonylalkynyl, alkynyl, carboxy, carboxyalkenyl, carboxyalkyl, carboxyalkynyl, haloalkoxy, haloalkyl, haloalkenyl, haloalkynyl, halogen, hydroxyalkyl, substituted amine; R5 is hydrogen, alkyl; R6 is hydrogen, alkoxycarbonyl, alkoxysulfonyl, alkyl, alkylcarbonyl, alkylsulfonyl, arylalkoxycarbonyl, arylalkylcarbonyl, arylalkylsulfonyl, arylcarbonyl, arylsulfonyl, cycloalkylcarbonyl, cycloalkylalkylcarbonyl, cycloalkylsulfonyl, cycloalkylalkylsulfonyl, heterocyclecarbonyl, heterocyclealkylcarbonyl, heterocyclesulfonyl, heterocyclealkylsulfonyl, amide, aminosulfonyl; X and Y are independently heteroatom-contg. hydrocarbon. Thus, N-[3-(dibenzylamino)-2-methylphenyl]ethanesulfonamide was prepd. as glucocorticoid receptor modulator. A method of treating symptoms related to type II diabetes wherein said symptoms are selected from the group consisting of hyperglycemia, hyperinsulinemia, inadequate glucose clearance, obesity, hypertension and high glucocorticoid levels in a mammal comprising administering a therapeutically effective amt. of a compd. of title compds. A method of treating diseases assocd. with an excess or deficiency of glucocorticoids, said diseases selected from the group consisting of diabetes, obesity, Syndrome X, Cushing's Syndrome, Addison's disease, inflammatory diseases such as asthma, rhinitis and arthritis, allergy, autoimmune disease, immunodeficiency, anorexia, cachexia, bone loss or bone frailty, and wound healing comprising administering a therapeutically effective amt. of a compd. of title compds.

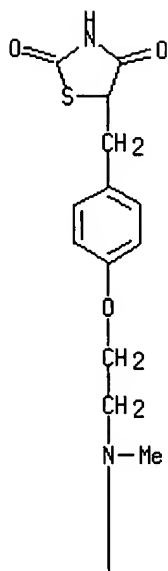
IT 122320-73-4, Rosiglitazone

RL: BSU (Biological study, unclassified); BIOL (Biological study) (prepn. of substituted aminobenzene derivs. as glucocorticoid receptor modulators)

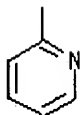
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:780683 HCAPLUS

DOCUMENT NUMBER: 135:335156

TITLE: Modified-release formulations containing a hypnotic agent

INVENTOR(S): Platteeuw, Johannes Jan; Van Den Heuvel, Dennie Johan Marijn; Van Dalen, Frans; Lemmens, Jacques Maria

PATENT ASSIGNEE(S): Synthron B.V., Neth.

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|----------------------|----|----------|----------------------|----------|
| <u>WO 2001078725</u> | A2 | 20011025 | <u>WO 2001-NL299</u> | 20010412 |
|----------------------|----|----------|----------------------|----------|

| | | | | |
|----------------------|----|----------|--|--|
| <u>WO 2001078725</u> | A3 | 20011220 | | |
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CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
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 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-196939P P 20000413

AB Hypnotic pharmaceutical compns. are made from pellets and exhibit a modified release. Zolpidem or a pharmaceutically acceptable salt thereof is a typical hypnotic. The pellets are preferably spherical and exhibit a dissoln. profile that includes 60% of the hypnotic agent being released from the pellet not earlier than 5 min from the start of a specified in vitro dissoln. test. Although the modified release profile can include 50 of the hypnotic agent being released not earlier than 15 min after the start of the dissoln. test, the pellet preferably does not contain a release rate controlling excipient or coating. Instead, microcryst. cellulose and the active constitute the majority of the pellet, e.g. 90 or more. Spherical pellets are also made by a convenient method that is applicable to any pharmaceutically active agent. Microcryst. cellulose 1703, zolpidem **hydrochloride hydrate** 189.2 g, and water 1892 mL were mixed and stirred for 15 min. Water was then removed and the resulted pellets were dried and fractionated by sieving.

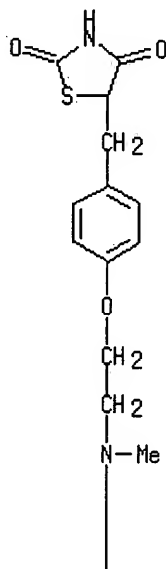
IT 122320-73-4, Rosiglitazone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (modified-release formulations contg. hypnotic agent)

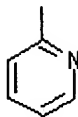
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
 hyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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L6 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:693320 HCAPLUS
DOCUMENT NUMBER: 135:247196
TITLE: Preparation of non-hygroscopic **hydrochloride** salts
of 5-[4-[2-(n-methyl-n-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione
INVENTOR(S): Craig, Andrew Simon
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001068646 A1 20010920 WO 2001-GB1131 20010314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-6133 A 20000314

AB A substantially non-hydrated and non-hygroscopic or slightly hygroscopic **hydrochloride** salts of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I); a pharmaceutical compn. contg. such a compd., a process of prepg. such a compd. and the use of such a compd. in medicine is disclosed. I was prepd. by the reaction of HCl with the base, m.p. = 167-170. I was non-hygroscopic.

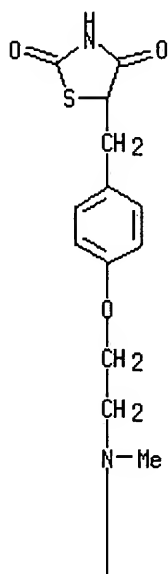
IT 302543-62-0P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-hygroscopic **hydrochloride** salts of pyridylaminoethoxybenzyl thiazolidinedione)

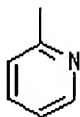
RN 302543-62-0 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:338762 HCAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001032928 A2 20010510 WO 2000-US30474 20001103

WO 2001032928 A3 20020725

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

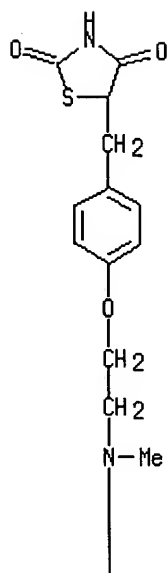
IT 122320-73-4, Rosiglitazone

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

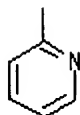
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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L6 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2001:283949 HCAPLUS

DOCUMENT NUMBER: 134:311218

TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors

INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 221 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|------|----------|------------------------|----------|
| <u>WO 2001027107</u> | A2 | 20010419 | <u>WO 2000-US27461</u> | 20001002 |
| <u>WO 2001027107</u> | A3 | 20020124 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1224183 A2 20020724 EP 2000-968723 20001002

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IE, SI, LT, LV, FI, RO, MK, CY, AL

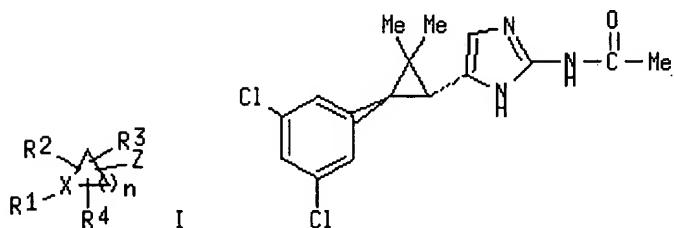
NO 2002001717 A 20020610 NO 2002-1717 20020411

PRIORITY APPLN. INFO.: US 1999-158755P P 19991012

WO 2000-US27461 W 20001002

OTHER SOURCE(S): MARPAT 134:311218

GI



AB Compds. of formula I [wherein; n is 1-5; X is N or CR₅, where R₅ is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R₁ is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)₃Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R₂, R₃ and R₄ are any of the groups set out for R₁ and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R₁ is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding α-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, β-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT 122320-73-4, Rosiglitazone

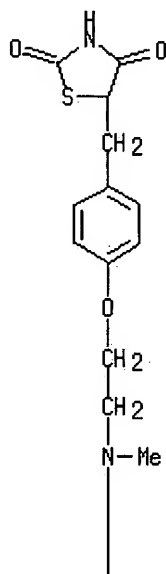
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

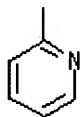
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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L6 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2000:756704 HCAPLUS

DOCUMENT NUMBER: 133:325652

TITLE: 5-[4-[2-(N-Methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione **hydrochloride** monohydrate
pharmaceutical

INVENTOR(S): Blackler, Paul David James; Craig, Andrew Simon;
Giles, Robert Gordon; Sasse, Michael John

PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK

SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000063206 A2 20001026 WO 2000-GB1527 20000419

WO 2000063206 A3 20010222

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1173437 A2 20020123 EP 2000-920895 20000419

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

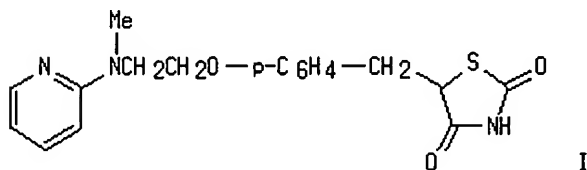
BR 2000009898 A 20020416 BR 2000-9898 20000419

NO 2001005105 A 20011219 NO 2001-5105 20011019

PRIORITY APPLN. INFO.: GB 1999-9075 A 19990420

WO 2000-GB1527 W 20000419

GI



AB 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione **hydrochloride** monohydrate (I.HCl.H₂O) is characterized in that it: (i) provides an IR spectrum contg. peaks at 3358, 2764, 1245, 833 and 760 cm⁻¹; and/or (ii) provides an XRPD pattern contg. peaks at 15.0, 17.7, 23.0, 30.0 and 31.4 >2303082-83-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

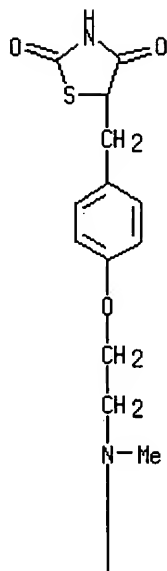
BIOL (Biological study); PREP (Preparation); USES (Uses)

(5-[4-[2-(N-Methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione **hydrochloride** monohydrate pharmaceutical)

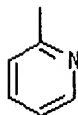
RN 303082-83-9 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monohydrochloride, monohydrate (9CI) (CA INDEX NAME)

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PAGE 2-A



HCl

H₂O

=> file caold

| COST IN U.S. DOLLARS | ENTRY | SINCE FILE SESSION | TOTAL |
|----------------------|-------|--------------------|--------|
| FULL ESTIMATED COST | | 32.75 | 241.48 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | ENTRY | SINCE FILE SESSION | TOTAL |
|--|-------|--------------------|--------|
| CA SUBSCRIBER PRICE | | -3.72 | -12.39 |

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FILE COVERS 1907-1966
 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L1 STRUCTURE UPLOADED
L2 2 S L1
L3 48 S L1 FULL

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L4 490 S L3
L5 14 S L4 AND HYDRA?

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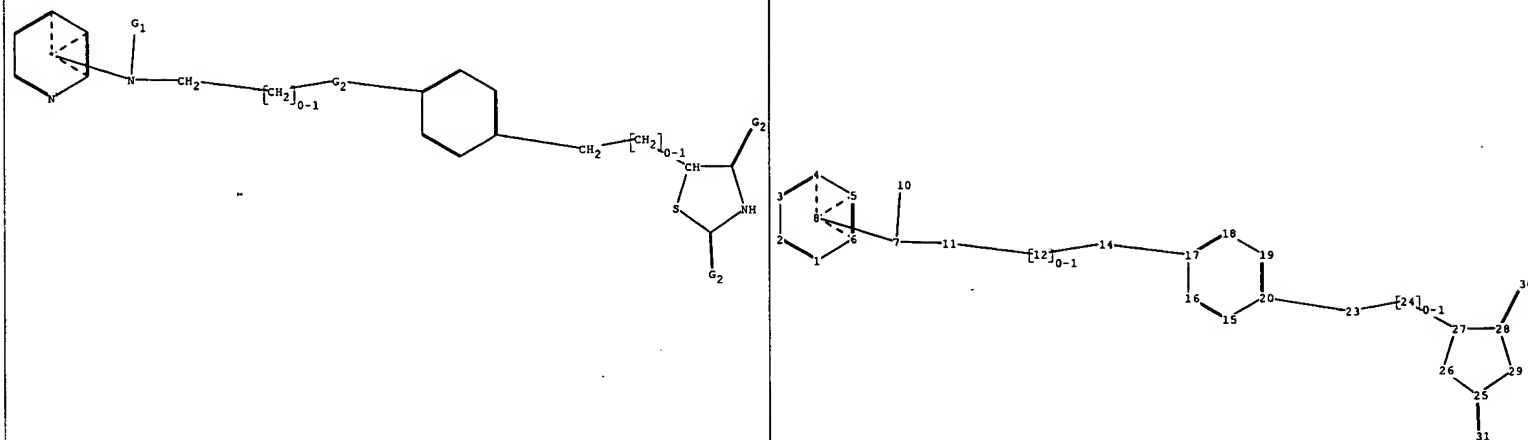
L6 6 S L5 AND HYDROCHLORIDE

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=> s l3

L7 0 L3

=>



chain nodes :

7 10 11 12 14 23 24 30 31

ring nodes :

1 2 3 4 5 6 15 16 17 18 19 20 25 26 27 28 29

chain bonds :

7-10 7-11 11-12 12-14 14-17 20-23 23-24 24-27 25-31 28-30

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 25-26 25-29
26-27 27-28 28-29

exact/norm bonds :

7-10 12-14 14-17 25-29 25-31 28-29 28-30

exact bonds :

7-11 11-12 20-23 23-24 24-27 25-26 26-27 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20

isolated ring systems :

containing 1 : 15 : 25 :

G1:CH3,Et

G2:O,S

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 10:CLASS 11:CLASS
12:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 23:CLASS
24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:CLASS 31:CLASS